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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/921,144	08/01/2001	Caili Wang	13403.0004.NPUS00	6422

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04/11/2003

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EXAMINER

HELMS, LARRY RONALD

ART UNIT

PAPER NUMBER

1642

10

DATE MAILED: 04/11/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/921,144

Applicant(s)

WANG ET AL.

Examiner

Larry R. Helms

Art Unit

1642

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 05 February 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-93 is/are pending in the application.
- 4a) Of the above claim(s) 31-86 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-30 and 87-93 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 5.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☒ Other: *notice to comply*.

DETAILED ACTION

Election/Restrictions

1. Applicant's election without traverse of Group I, claims 1-30 and 87-93 in Paper No. 9 is acknowledged.
2. Claims 31-86 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Election was made **without** traverse in Paper No. 9.
3. Claims 1-30, 87-93 are under examination.

Specification

4. The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code, see for example page 38, line 16. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.
5. The disclosure is objected to because of the following informalities: The specification should include a SEQ ID NO for all sequences listed in the specification.
Appropriate correction is required.

Sequence Requirements

6. Although a search and a first action on the merits could be performed on the application, this application contains sequences for example on page 71 paragraph 202

that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 C.F.R. § 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 C.F.R. §§ 1.821-1.825 for the reason(s) set forth IN THE Notice to Comply.

Any questions regarding compliance with the sequence rules requirements specifically should be directed to the departments listed at the bottom of the Notice to Comply.

APPLICANT IS GIVEN THE TIME ALLOTTED IN THIS LETTER WITHIN WHICH TO COMPLY WITH THE SEQUENCE RULES, 37 C.F.R. §§ 1.821-1.825.

Failure to comply with these requirements will result in ABANDONMENT of the application under 37 C.F.R. § 1.821(g). Extensions of time may be obtained by filing a petition accompanied by the extension fee under the provisions of 37 C.F.R. § 1.136. In no case may an applicant extend the period for response beyond the six month statutory period. Direct the response to the undersigned. Applicant is requested to return a copy of the attached Notice to Comply with the response.

Claim Rejections - 35 USC § 112

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 1-30, 87-93 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a. Claim 3, 22, and those that depend on claims 3 and 22 are indefinite for reciting "sequences that mediate heterodimerization of the receptors" because the exact meaning of the phrase is not clear. It is not clear if the term "receptors" is used to modify the heterodimeric receptor sequences. In addition, it is not clear if the heterodimeric receptor sequences are from the same receptor or different receptor sequences.

b. Claims 1-30, 87-93 are indefinite for reciting the term "sequences" because the term "sequence" refers to information describing the amino acid sequence. Information is not a chemical structure, therefore, it is not clear how "sequences" can be linked to a cysteine residue. Replacing this term with polypeptide, would be sufficient to obviate this part of the rejection.

c. Claims 8, 18, 19, 29-30 and those claims that depend from these claims are indefinite for reciting "first and second heterodimerization sequences are linked to at least one cysteine residue" because the exact meaning of the phrase is not clear. It is not clear if the first and second heterodimerization amino acid sequences are linked to each other by a disulfide bond or if the heterodimerization amino acids sequences are connected to the VL or VH by a cysteine residue.

d. Claims 18, 19, 29-30 and those that depend from these claims are indefinite for reciting "essentially identical" and "comparable length" because the exact meaning of the phrases are not clear. It is not clear what differences in the amino acids results in a sequence that are "essentially identical" and it is not clear what "comparable length" is

in light that if one peptide is 30 amino acids is "comparable length" 45 amino acids for the polypeptide?

e. Claims 17, 26-28 are indefinite for reciting "derived". The term "derived" is not one which has a universally accepted meaning in the art nor is it one which has been adequately defined in the specification. The specification defines "derived from" as designating the protein to the origin of the polypeptide (see page 18, lines 65-67) but does not describe what changes are encompassed by the term "derive". The primary deficiency in the use of this phrase is the absence of a ascertainable meaning for said phrase. Since it is unclear how the sequences are to be derivatized to yield the class of derivatives referred to in the claims, there is no way for a person of skill in the art to ascribe a discrete and identifiable class of compounds to said phrase. In addition, the term can encompass proteins with amino acid substitutions, insertions, or deletions, antibody fragments, chemically derivatized molecules, or even antibody mimetics. In absence of a single defined art recognized meaning for the phrase and lacking a definition of the term in the specification, one of skill in the art could not determine the metes and bounds of the claims.

f. Claims 20 and 22 and those that depend from claims 20 and 22 are indefinite for reciting "a first and a second heterodimerization sequences spanning the distance between the C-terminus of one of the region to the N-terminus of the other region" because the exact meaning of the phrase is not clear. Does the phrase mean that the VL and the VH are connected by the first and second heterodimerization domains (see below) or are the VH and VL connected by a linker and the heterodimerization domains

connect the VH to the VL or does the heterodimerization domain connect two single-chain unit (see below)? In addition does the term "spanning the distance" mean the heterodimerization domain is long enough to connect the VH or VL or does the phrase mean that the dimerization domain is as long as the VH and VL? In addition, it is not clear if the first and the second heterodimerization sequences are the same or different.

VH-first domain-second domain-VL or VH-VL-first domain-second domain (where the VH attaches to the second domain) or VH-VL-first domain second domain VH-VL

Claim Rejections - 35 USC § 102

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

10. Claims 20-21, 23-27 are rejected under 35 U.S.C. 102(b) as being anticipated by Pluckthun et al (Immunotechnology 3:83-105, 1997).

The claims recite a single chain antigen binding unit which is humanized comprising a light chain and a heavy chain connected by a first and a second heterodimerization domain which spans the C terminus to N terminus wherein at least one heterodimerization domain is incapable of forming a homodimer under physiological buffer conditions and wherein the heterodimerization domains are coiled-coil and

dimerize via no-covalent affinity. Further the antigen binding unit is conjugated to a functional moiety. Due to the indefinite nature of claim 20 it is being interpreted as a single chain antigen binding unit connected to a dimerization domain (VH-VL-domain domain-VH-VL).

Pluckthun et al teach dimeric antibodies and humanized antibodies wherein the antibodies comprise a single chain antigen binding unit comprising a VH and a VL connected to a dimerization coiled-coil domain and the dimerization domains are long enough to span the C terminus to N terminus of the scfv (see Figure 3). Pluckthun et al also teach that careful modification of the coiled-coil sequences leads to heterodimerization over homodimerization in E.coli at host temperatures (see page 99) and the addition of effector moieties (see page 101).

Conclusion

11. No claim is allowed.
12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Larry R. Helms, Ph.D, whose telephone number is (703) 306-5879. The examiner can normally be reached on Monday through Friday from 7:00 am to 4:30 pm, with alternate Fridays off. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, can be

reached on (703) 308-3995. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

13. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 308-4242.

Respectfully,

Larry R. Helms Ph.D.

703-306-5879

A handwritten signature in black ink, consisting of several sweeping, overlapping strokes that form a stylized representation of the name Larry R. Helms.